

WHAT IS CLAIMED IS:

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1. A method for the induction of p53-mediated apoptosis in a cell comprising the step of contacting a cell with at least one inhibitory agent that inhibits DNA repair.

2. The method of claim 1, further comprising contacting said cell with a first stimulatory agent that increases the level of a tumor suppressor in said cell.

3. The method of claim 2, wherein said tumor suppressor is selected from the group consisting of p53, p21 and MSH-2.

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4. The method of claim 2, wherein said first stimulatory agent is an expression construct that comprises a nucleic acid encoding a tumor suppressor under the control of a promoter active in eukaryotic cells.

5. The method of claim 4, wherein said tumor suppressor is p53.

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6. The method of claim 5, wherein said expression construct is an adenoviral expression construct.

7. The method of claim 6, wherein said adenoviral expression construct lacks a portion of at least one gene essential to adenoviral replication.

8. The method of claim 7, wherein the essential gene is E1.

9. The method of claim 4, wherein said promoter is a CMV promoter.

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10. The method of claim 1, wherein said inhibitory agent inhibits the function of a protein selected from the group consisting of c-jun, c-fos, poly-ADP ribose polymerase, DNA polymerase β , topoisomerase I, d-TMP synthase, hMTII-A, uracil DNA glycosylase, alkyl-N-purine DNA glycosylase, DNA ligase IV, DNA

ligase III, Hap-1, Ref-1, poly-ADP ribose polymerase and DNA-dependent protein kinase.

5 11. The method of claim 10, wherein said inhibitory agent is a competitor of a gene product selected from the group consisting of c-jun, c-fos, poly-ADP ribose polymerase, DNA polymerase β , topoisomerase I, d-TMP synthase, hMTII-A, uracil DNA glycosylase, alkyl-N-purine DNA glycosylase, DNA ligase IV, DNA ligase III, Hap-1, Ref-1, poly-ADP ribose polymerase and DNA-dependent protein kinase.

10 12. The method of claim 10, wherein said inhibitory agent is an antisense construct encoding at least a portion of a gene selected from the group consisting of c-jun, c-fos, poly-ADP ribose polymerase, DNA polymerase β , topoisomerase I, d-TMP synthase, hMTII-A, uracil DNA glycosylase, alkyl-N-purine DNA glycosylase, DNA ligase IV, DNA ligase III, Hap-1, Ref-1, poly-ADP ribose polymerase and DNA-dependent protein kinase.

15 13. The method of claim 10, wherein said inhibitory agent is a retinoid.

14. The method of claim 13, wherein said retinoid is the synthetic retinoid SR11220.

15. The method of claim 10, wherein said inhibitory agent is 3-aminobenzamide.

20 16. The method of claim 1, further comprising the step of providing a DNA-damaging agent.

25 17. The method of claim 16, wherein said DNA-damaging agent is selected from the group consisting of cisplatin, carboplatin, VP16, teniposide, daunorubicin, doxorubicin, dactinomycin, mitomycin, plicamycin, bleomycin, procarbazine, nitrosourea, cyclophosphamide, bisulfan, melphalan, chlorambucil,

ifosfamide, merchlorhtamine, taxol, taxotere, anthracyclines and ionizing radiation.

18. The method of claim 1, wherein said cell is a tumor cell.

19. The method of claim 18, wherein said tumor cell is selected from the group consisting of lung tumor cell, a prostate tumor cell, a breast tumor cell, a colon tumor cell, a liver tumor cell, a brain tumor cell, a kidney tumor cell, a skin tumor cell and an ovarian tumor cell.

20. The method claim 18, wherein said tumor cell is selected from the group consisting of a squamous cell carcinoma, a non-squamous cell carcinoma, a glioblastoma, a sarcoma, a melanoma, a papilloma, a neuroblastoma and a leukemia cell.

21. The method of claim 1, wherein said tumor cell is in a subject.

22. The method of claim 1, wherein said subject is human.

23. The method of claim 1, wherein said inhibitory agent is delivered by direct intratumoral injection.

24. The method of claim 2, wherein said stimulatory agent is delivered by direct intratumoral injection.

25. The method of claim 23, wherein said injection comprises continuous perfusion.

26. The method of claim 24, wherein said injection comprises continuous perfusion.